REMARKS

With entry of the present amendments, claims 1-38, 49-51, 53-58, 67, and 69-71 are pending in the application. Claims 1, 9, 30, 36, 49, 53, 67, and 69-71 have been amended and claim 68 has been cancelled. No new matter is introduced by the amendment as the amended language is supported by the application as originally filed. Applicants respectfully request reconsideration of the present application in view of the foregoing amendment and in view of the reasons that follow.

As an initial matter, Applicants thank the Examiner for withdrawing the previously issued rejections under 35 U.S.C. § 112, first paragraph.

I. Rejections under 35 U.S.C. § 103(a)

Claims 1-6, 9-13, 16-38, 49-51, 53-58, and 67-71 stand rejected under 35 U.S.C. § 103(a) for allegedly being obvious over U.S. Pat. No. 6,605,617 issued to Renhowe et al. ("Renhowe") in view of "Guideline for the Format and Content of the Human Pharmacokinetic and Bioavailability Section of an Application" published by the FDA ("FDA Guidelines"). Claims 7-8 and 14-15 stand rejected under 35 U.S.C. § 103(a) for allegedly being obvious over Renhowe in view of the FDA Guidelines and in further view of a paper by Berge et al. ("Berge"). Cancellation of claim 68 renders the rejection moot with respect to this claim. Applicants respectfully traverse the rejection of the remaining claims.

As an initial matter, Applicants note that each of the independent claims 1, 9, 36, 49, and 53 have been amended to recite a method of treating very specific types of cancer—those cancers comprising cells that express the PDGFR, c-Kit, or FLT-3 receptor tyrosine kinase. Each of these kinases is a member of the PDGF class (Class III) of receptor tyrosine kinases.

Even assuming *arguendo* one of ordinary skill in the art were to combine the teachings of Renhowe, with one or both of the FDA Guidelines and Berge, Applicants respectfully submit that the combination fails to render obvious the claimed method for several reasons. First, the

combination of references fail to teach or suggest each and every element of independent claims 1, 9, 36, 49, and 53. As recognized by the Office, Renhowe teaches a genus of compounds that have been shown to inhibit three specific receptor tyrosine kinases, VEGFR1, VEGFR2, and bFGFR. Renhowe, col. 101, lines 45-47. Renhowe also teaches a method of treating diseases mediated by a VEGF receptor tyrosine kinase using the disclosed compounds. Renhowe, col. 1, lines 11-21; col. 3, lines 28-35; and claim 30. However, Renhowe fails to teach or suggest that the disclosed compounds are capable of inhibiting other types of receptor tyrosine kinases, and certainly fails to teach or suggest that the compounds are capable of inhibiting the specific kinases recited in the present claims. Accordingly, Renhowe cannot teach or suggest a method of treating cancers expressing such kinases as recited in the present claims.

Second, Renhowe provides insufficient basis to support any reasonable expectation that the compounds of Renhowe would be capable of inhibiting PDGFR, c-Kit, or FLT-3, or that the compounds would be capable of treating cancers expressing such kinases. As noted above, PDGFR, c-Kit, and FLT-3 are members of the PDGF class (Class III) of receptor tyrosine kinases—a class which is distinct from both the VEGF and FGF classes of receptor tyrosine kinases referenced in Renhowe. Inhibitors of one class of receptors do not necessarily inhibit another class of receptors. Similarly, not all cancers express the recited kinases, and a method of treating a cancer mediated by one type of kinase (e.g., a method of treating a cancer mediated by a VEGF receptor tyrosine kinase) does not necessarily provide a viable method for treating a cancer mediated by another type of receptor tyrosine kinase.

Third, regarding the Office's reference to col. 61, lines 11-14 of Renhowe and the comments spanning pp. 5 and 6 of the Office Action, Applicants respectfully submit that such a teaching is insufficient to render the presently claimed methods unpatentable. As the Federal Circuit established in *Metabolite Labs*, prior art references that do no more than disclose a broad genus of potential applications for their discoveries or invite further experimentation are generally insufficient to support a conclusion of unpatentability. ("[A]n invitation to investigate is not an inherent disclosure." *Metabolite Labs., Inc. v. Lab. Corp. of Am. Holdings* 71 USPQ2d

1081, 1091 (Fed. Cir. 2004).) As discussed above, nowhere in Renhowe is it demonstrated that the disclosed compounds inhibit the recited kinases or that such compounds provide a viable treatment for cancers expressing such kinases. Only the data disclosed in the present application teaches that these compounds possess such activity. Even if Renhowe invites further experimentation to discover other applications for the disclosed compounds, under *Metabolite Labs*, such a teaching is insufficient to render the present claims unpatentable.

Finally, Applicants note that each of the independent claims recites administration of a specific compound, 4-amino-5-fluoro-3-[6-(4-methylpiperazin-1-yl)-1*H*-benzimidazol-2-yl]quinolin-2(1*H*)-one (or salts, tautomers, metabolites, etc. thereof). Applicants respectfully submit that the Office has not explained why it would be obvious to the skilled artisan to select this particular compound from among the many compounds disclosed in Renhowe. Renhowe teaches a large genus of quinolinone derivative compounds. The recited compound, Example 109, is but one of hundreds of specific compounds disclosed in Renhowe. Aside from generally disclosing that the specific compounds displayed inhibitory effects against three receptors, VEGFR1, VEGFR2, and bFGFR (none of which is PDGFR, c-Kit, or FLT-3), the reference provides no guidance leading one of ordinary skill in the art to select the recited compound, or any other particular compound, from among the hundreds of possible choices. Thus, the selection of the claimed compound cannot be considered obvious.

Because nothing in the FDA guidelines or Berge cures any of the deficiencies in Renhowe described above, Applicants respectfully submit that the combination of references fails to provide a case of *prima facie* obviousness. Accordingly, Applicants respectfully request withdrawal of the present ground of rejection of independent claims 1, 9, 36, 49, and 53, and any claims depending therefrom.

II. Obviousness-type double-patenting rejection

Claims 1-6, 9-15, 16-38, 49-51, 53-58, and 67-71 stand rejected for alleged obviousness-type double-patenting (ODP) over claim 30 of Renhowe. Applicants respectfully traverse.

Applicants respectfully draw the Office's attention to the arguments set forth on pp. 14-18 of Applicants' Reply of November 16, 2007. These arguments relate to a previous ODP rejection over claims 30 of Renhowe—a rejection that was subsequently withdrawn in the Office Action dated February 7, 2008 (see page 2). For the Office's convenience, the relevant portions of these arguments are repeated below.

A proper ODP is based on an analysis that is similar to that of an obviousness rejection under 35 U.S.C. § 103, but must rely on what is taught in the claims of the cited patent. In this case, claim 30 simply teaches a method of treating a patient in need of a VEGF inhibitor using a very broad genus of quinolinone derivative compounds. In view of this limited teaching, the presently claimed methods must be considered non-obvious.

As discussed in Section I, above, nothing in Renhowe—and certainly nothing in claim 30 of Renhowe—teaches or suggest that the compounds recited in claim 30 are capable of inhibiting PDGFR, c-Kit, or FLT-3 kinases or that such compounds would be capable of treating cancers expressing such kinases. Similarly, for each of the reasons discussed above, neither the specification of Renhowe nor claim 30 of Renhowe provides sufficient basis to support any reasonable expectation that the compounds of claim 30 would possess such activities.

Moreover, the present claims recite a non-obvious selection of compounds encompassed by claim 30 of Renhowe. As noted above, claim 30 is directed to methods that recite an extremely large number of compounds. However, claim 30 fails to provide any guidance at all directing the skilled artisan to any particular compound in the recited genus, and certainly does not lead this artisan to the specific compounds recited in the present claims. As discussed at pp. 15-16 of Applicants' Reply of November 16, 2007, courts have found selection inventions to be patentably distinct where the prior art provides insufficient guidance for selecting a specific compound from a large genus. ("The fact that a claimed compound may be encompassed by a disclosed generic formula does not by itself render that compound obvious." *In re Baird*, 29 USPQ2d 1550, 1552 (Fed. Cir. 1994).)

For each of these reasons, Applicants respectfully submit that claim 30 of Renhowe fails to provide a *prima facie* case of obviousness. Accordingly, Applicants respectfully request withdrawal of the present ground of rejection of independent claims 1, 9, 36, 49, and 53, and any claims depending therefrom.

CONCLUSION

Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested. If any issues remain to be resolved in view of this amendment and reply, the Examiner is requested to contact the undersigned by telephone to achieve a prompt disposition thereof.

Respectfully submitted,

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